AMENDMENTS TO HUMAN GENE TRANSFER PROTOCOLS
RECOMBINANT DNA ADVISORY COMMITTEE
MARCH 10, 1998

11-20-97 (letter date)	**9706-191 Gluckman *et al.***	**Phase II Study of Immunotherapy by Direct Gene Transfer with Allovectin-7 for the Treatment of Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck** **Amendment:** One principal investigator/site is added to the protocol.The PI at the new site; University of Michigan Medical Center; Ann Arbor, Michigan; is Gregory T. Wolf, M.D.
12-2-97	**9409-088 Isner and Walsh**	**Arterial Gene Transfer for Therapeutic Angiogenesis in Patients with Peripheral Artery Disease** **Amendment:** Received reversed protocol from PI, Dr.Isner, for intramuscular gene transfer of naked DNA encoding for vascular endothelial growth factor in patients with peripheral artery disease. Dr. Isner stated "...that this protocol was pursued as an amendment to the intr-arterial protocol. The only remarkable difference between the two protocols is the route of administration. The plasmid vector is the same and the clinical endpoints are unchanged".
12-4-97	**9706-196 Smith and Dinauer**	**Fibronectin-Assisted, Retroviral-Mediated Transduction of CD34+ Peripheral Blood Cell with gp91 phox in Patients with X-Linked Chronic Granulomatous Disease: A Phase I Study** **Amendments:** Minor amendments have been made to the clinical protocol. 1) Patients will undergo aphereis for a maximum of two days. 2) New "stratification." If number of cells, peripheral blood progenitor cells, collected exceeds 7.5×10^8, patients will receive both fresh and cryopreserved transduced cells. If the number is less than 7.5×10^8 cells, patients will only receive fresh cells.In either case, at most two transfusions will be done. One transfusion of fresh cells and if possible one transfusion, six months later, of cryopreserved transduced cells. 3) Other changes in the cryoprservation procedure and the transduction procedure have

		been made to reflect the new "stratification."
12-12-97	**9703-184 Belldegrun**	**A Phase I Study Evaluating the Safety and Efficacy of Interleukin-2 Gene Therapy Delivered by Lipid Mediated Gene Transfer (Leuvectin) in Prostate Cancer Patients** **Amendments:** 1) Pre-treatment biopsy has been added to obtain a baseline for comparison to the post-treatment biopsy. 2) Change in the inclusion criteria so that creatinine levels must now be in the normal range instead of less than 0.8mg/dL.
12-15-97	**9709-214 Breau *et al.***	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN)** **Amendment:** Two principal investigators/sites are added to the protocol. The new PIs are David E. Schuller, M.D. at Ohio State University Medical Center; Columbus, Ohio; and Ronald M. Bukowski, M.D. at The Cleveland Clinic Foundation; Cleveland, Ohio.
12-22-97	**9706-191 Gluckman *et al.***	**Phase II Study of Immunotherapy by Direct Gene Transfer with Allovectin-7 for the Treatment of Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck** **Amendment:** One principal investigator/site is added to the protocol. The PI at the new site; Mayo Clinic; Rochester, Minnesota; is Scott Okuno, M.D.
1-6-98	**9706-191 Gluckman *et al***	**Phase II Study of Immunotherapy by Direct Gene Transfer with Allovectin-7 for the Treatment of Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck** **Amendment:** To allow investigation of the effects of Allovectin-7 in patients with advance or recurrent non-squamous cell cancer of the head and neck or aerodigestive tract. Patients with certain skin cancers such as melanoma or basal cell carcinoma are excluded. The amendment will initially be conducted at the U. of Cincinnati Medical Center by Dr. Jack Gluckman. The amendment has been approved by the U. of Cincinnati IBC and IRB.
	9406-078	**Retroviral Mediated Gene Transfer of the Franconi Anemia Complementation Group**

1-7-98	**Johnson and Young**	**C Gene to Hematopoietic Progenitors of Group C Patients Amendments:** 1) Transduce autologous hematopoietic progenitor and stem cells isolated from bone marrow rather than from mobilized peripheral blood in 3 patients. 2) One principal investigator/site is added to the protocol. The PI at the new site; University of Minnesota; Minneapolis, Minnesota; is John E. Wagner, M.D.
1-30-98	**9701-173 Williams**	**A Pilot Study of Dose Intensified Procarbazine, CCNU, Vincristine (PCV) for Poor Prognosis Pediatric and Adult Brain Tumors Utilizing Fibronectin-Assisted, Retroviral-Mediated Modification of CD34+ Peripheral Blood Cells with O^6-Methylguanine DNA Methyltransferase** **Amendments:** Changes have been made to the eligibility criteria to state more clearly the types of poor prognosis brain tumor patients who may enroll in the study. Minor changes have been made to the clinical protocol to reduce confusion with respect to the eligibility of patients currently undergoing radiation therapy. The protocol has been amended to allow admission of patients either prior to radiation therapy or following completion of radiation therapy. The investigators state that: "We do not anticipate that timing of radiation therapy in relation to the chemotherapy/stem cells would affect the objectives of the study, nor do we anticipate that the proposed revisions will effect the risk/benefit ratio for the patients".
2-13-98	**9709-212 Gonzalez *et al.***	**Phase I Study of Direct Gene Transfer of HLA-B7 Plasmid DNA/DMRIE/DOPE Lipid Complex (Allovectin-7) with IL-2 Plasmid DNA/DMRIE/DOPE Lipid Complex (Leuvectin) as an Immunotherapeutic Regimen in Patients with Metastatic Melanoma** **Amendment:** One principal investigator/site is added to the protocol. The PI at the new site; Mayo Clinic; Rochester, Minnesota; is Joseph Rubin, M.D.
2-13-98	**9608-157 Maria *et al.***	**Prospective, Open-Label, Parallel-Group, Randomized Multicenter Trial Comparing the Efficacy of Surgery, Radiation, and Injection of Murine Cells Producing Herpes Simplex Thymidine Kinase Vector Followed by Intravenous Ganciclovir Against the Efficacy of Surgery and Radiation in the Treatment of Newly Diagnosed, Previously Untreated Glioblastoma**

		Amendments: 1) Dr. John Gutheil has replaced Dr. Ivor Royston as the PI at the Sharp HealthCare/Sidney Kimmell Cancer Center and Dr. Martti Kulvik has replaced Dr. Leena Kivipelto as the PI at Helsinki University Central Hospital 2) Three principal investigators/sites are added to the protocol.The PI at Universitatsklinik fur Neurologie is Gunther Stockhammer, M.D.; the PI at Centre Leon Berard is Professeur Marie Favrot; and the PI at Unita' Neuroncologia Molecolare e Terapia Genica is Dr. Gaetano Finocchiaro.
2-17-98	**9709-214 Breau *et al.***	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with RecurrentSquamous Cell Carcinoma of the Head and Neck (SCCHN) Amendment:** One principal investigator/site is added to the protocol.The PI at the new site; University of Louisville Health Sciences Center; Louisville, Kentucky; is John Hamm, M.D.